**INDICATIONS AND USAGE**

VICTOZA® is a glucagon−like peptide−1 (GLP−1) receptor agonist indicated:
- as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus (1).
- to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease (1).

**Limitations of Use:**
- Not for treatment of type 1 diabetes mellitus.
- Should not be coadministered with other liraglutide-containing products.
- Should not be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (8.1).

**DOSAGE AND ADMINISTRATION**

- Adult Patients: Initiate at 0.6 mg injected subcutaneously once daily for one week then increase to 1.2 mg daily. If additional glycemic control is required, increase the dose to 1.8 mg daily after one week of treatment with the 1.2 mg daily dose (2.1).
- Pediatric Patients: Initiate at 0.6 mg injected subcutaneously once daily for at least one week. If additional glycemic control is required increase the dose to 1.2 mg daily and if additional glycemic control is still required, increase the dose to 1.8 mg daily after at least one week of treatment with the 1.2 mg daily dose (2.1).
- Inspect visually prior to each injection. Only use if solution is clear, colorless, and contains no particles (2.3).
- Inject VICTOZA® subcutaneously once-daily at any time of day, independently of meals, in the abdomen, thigh or upper arm (2.3).
- When using VICTOZA® with insulin, administer as separate injections. Never mix. (2.3).

**DOSE FORMS AND STRENGTHS**

Injection: 6 mg/mL solution in a pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg (3).

**DRUG INTERACTIONS**

- Effects of delayed gastric emptying on oral medications: VICTOZA delays gastric emptying and may impact absorption of concomitantly administered oral medications (7).

**CONTRAINICATIONS**

- Pregnancy: VICTOZA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (8.1).

See 17 for PATIENT COUNSELING INFORMATION and FDA-Approved Medication Guide. Revised: 07/2023
VICTOZA® (liraglutide) injection 1.2 mg, 1.8 mg

FULL PRESCRIBING INFORMATION

WARNING: RISK OF THYROID C-CELL TUMORS

• Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether VICTOZA® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined [see Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)].

• VICTOZA® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of VICTOZA® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with VICTOZA® [see Contraindications (4) and Warnings and Precautions (5.1)].

1 INDICATIONS AND USAGE

VICTOZA® is indicated:

• as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus,

• to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use:

VICTOZA® should not be used in patients with type 1 diabetes mellitus.

VICTOZA® contains liraglutide and should not be coadministered with other liraglutide-containing products.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Adult Patients

• The recommended starting dosage of VICTOZA® is 0.6 mg injected subcutaneously once daily for one week. The 0.6 mg once daily dosage is intended to reduce gastrointestinal symptoms [see Adverse Reactions (6.1)] during initial titration and is not effective for glycemic control in adults.

• After one week at the 0.6 mg once daily dosage, increase the dosage to 1.2 mg injected subcutaneously once daily.

• If additional glycemic control is required, increase the dosage to the maximum recommended dosage of 1.8 mg injected subcutaneously once daily after at least one week of treatment with the 1.2 mg once daily dosage.

Pediatric Patients Aged 10 Years and Older

• The recommended starting dosage of VICTOZA® is 0.6 mg injected subcutaneously once daily.

• If additional glycemic control is required, increase the dosage in 0.6 mg increments after at least one week on the current dosage.

• The maximum recommended dosage is 1.8 mg injected subcutaneously once daily.

2.2 Recommendations Regarding Missed Dose

• Instruct patients who miss a dose of VICTOZA® to resume the once-daily dosage regimen as prescribed with the next scheduled dose. Do not administer an extra dose or increase the dose to make up for the missed dose.

• If more than 3 days have elapsed since the last VICTOZA® dose, reinitiate VICTOZA® at 0.6 mg once daily to mitigate any gastrointestinal symptoms associated with reinitiation of treatment. Upon reinitiation, VICTOZA® should be titrated at the discretion of the healthcare provider.

2.3 Important Administration Instructions

• Inspect visually prior to each injection. Only use if solution is clear, colorless, and contains no particles.

• Inject VICTOZA® subcutaneously once daily at any time of day, independently of meals.

• Inject VICTOZA® subcutaneously in the abdomen, thigh or upper arm. No dosage adjustment is needed if changing the injection site and/or timing.

• Rotate injection sites within the same region in order to reduce the risk of cutaneous amyloidosis [see Adverse Reactions (6.2)].

• When using VICTOZA® with insulin, administer as separate injections. Never mix. It is acceptable to inject VICTOZA® and insulin in the same body region but the injections should not be adjacent to each other.

3 DOSAGE FORMS AND STRENGTHS

Injection: 18 mg/3 mL (6 mg/mL) clear, colorless solution in a pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg.

4 CONTRAINDICATIONS

VICTOZA® is contraindicated in patients with a:

• personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see Warnings and Precautions (5.1)].

• serious hypersensitivity reaction to liraglutide or to any of the excipients in VICTOZA®. Serious hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with VICTOZA® [see Warnings and Precautions (5.6)].

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Thyroid C-Cell Tumors

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice [see Nonclinical/Toxicology (13.1)]. Malignant thyroid C-cell carcinomas were detected in rats and mice. It is unknown whether VICTOZA® will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in patients treated with VICTOZA® have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and VICTOZA® use in humans.

VICTOZA® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of VICTOZA® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with VICTOZA® [see Contraindications (4) and Warnings and Precautions (5.1)].

5.2 Pancreatitis

Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with VICTOZA®. After initiation of VICTOZA®, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, VICTOZA® should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, VICTOZA® should not be restarted.

In glycemic control trials of VICTOZA®, there have been 13 cases of pancreatitis among VICTOZA®-treated patients and 1 case in a comparator (glimepiride) treated patient (2.7 vs. 0.5 cases per 1000 patient years). Nine of the 13 cases with VICTOZA® were reported as acute pancreatitis and four were reported as chronic pancreatitis. In one case in a VICTOZA®-treated patient, pancreatitis, with necrosis, was observed and led to death, however clinical causality could not be established. Some patients had other risk factors for pancreatitis, such as a history of cholelithiasis or alcohol abuse.

VICTOZA® has been studied in a limited number of patients with a history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on VICTOZA®.

5.3 Never Share a VICTOZA® Pen Between Patients

VICTOZA® pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood-borne pathogens.

5.4 Hypoglycemia

Adult patients receiving VICTOZA® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. In pediatric patients 10 years of age and older, the risk of hypoglycemia was higher with VICTOZA® regardless of insulin and/or metformin use [see Adverse Reactions (6.1), Drug Interactions (7.2)]. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogues) or insulin. Inform patients using these concomitant medications and pediatric patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.

5.5 Acute Kidney Injury

VICTOZA® has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis in VICTOZA®-treated patients [see Adverse Reactions (6.2)]. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration [see Adverse Reactions (6.1)]. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or hydration status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including VICTOZA®. Use caution when initiating or escalating doses of VICTOZA® in patients with renal impairment [see Use in Specific Populations (8.6)].

5.6 Hypersensitivity Reactions

There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with VICTOZA® [see Adverse Reactions (6.2)]. If a hypersensitivity reaction occurs, discontinue VICTOZA®; treat promptly per standard of care, and monitor until signs and symptoms resolve.

Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-receptor agonist because it is unknown whether such patients will be predisposed to these reactions with VICTOZA®. VICTOZA® is contraindicated in patients who have had a serious hypersensitivity reaction to liraglutide or any of the excipients in VICTOZA® [see Contraindications (4)].

5.7 Acute Gallbladder Disease

Acute events of gallbladder disease such as cholelithiasis or cholecystitis have been reported in GLP-1 receptor agonist trials and postmarketing. In the LEADER trial [see Clinical Studies (14.3)], 3.1% of VICTOZA®-treated patients versus 1.9% of placebo-treated patients reported an acute event of gallbladder disease, such as cholelithiasis or cholecystitis [see Adverse Reactions (6.1)]. If cholecystitis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

• Risk of Thyroid C-Cell Tumors [see Warnings and Precautions (5.1)]

• Pancreatitis [see Warnings and Precautions (5.2)]

• Hypoglycemia [see Warnings and Precautions (5.4)]

• Acute Kidney Injury [see Warnings and Precautions (5.5)]

• Hypersensitivity Reactions [see Warnings and Precautions (5.6)]

• Acute Gallbladder Disease [see Warnings and Precautions (5.7)]
6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Common Adverse Reactions

The safety of VICTOZA® in patients with type 2 diabetes mellitus was evaluated in 5 glycemic control, placebo-controlled trials in adults and one trial of 52 weeks duration in pediatric patients 10 years of age and older (see Clinical Studies (14.1)). The data in Table 1 reflect exposure of 1,673 adult patients to VICTOZA® and a mean duration of exposure to VICTOZA® of 37.3 weeks. The mean age of adult patients was 58 years, 4% were 75 years or older and 54% were male. The population was 78% White, 6% Black or African American, 13% Asian; 4% were of Hispanic or Latino ethnicity. At baseline the population had diabetes for an average of 9 years and 9% had HbA1c of 8.4%. Baseline estimated renal function was normal or mildly impaired in 88% and moderately impaired in 12% of the population.

Table 1 shows common adverse reactions in adults, excluding hypoglycemia, associated with the use of VICTOZA® for the treatment of type 2 diabetes mellitus. These adverse reactions occurred more commonly on VICTOZA® than on placebo and occurred in at least 5% of patients treated with VICTOZA®. Overall, the type, and severity of adverse reactions in pediatric patients 10 years of age and older and above were comparable to that observed in the adult population.

<table>
<thead>
<tr>
<th>Common Adverse Reaction</th>
<th>Placebo N = 665</th>
<th>Liraglutide 1.2 mg N = 645</th>
<th>Liraglutide 1.8 mg N = 1024</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>5</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Headache</td>
<td>7</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>1</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>1</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>6</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Constipation</td>
<td>1</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Back Pain</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo N = 161</th>
<th>Liraglutide 1.2 mg N = 645</th>
<th>Liraglutide 1.8 mg N = 1024</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
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<td>Constipation</td>
<td>1</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Back Pain</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Cumulative proportions were calculated combining studies using Cochran-Mantel-Haenszel weights.

Other Adverse Reactions

Gastrointestinal Adverse Reactions

In the pool of 5 glycemic control, placebo-controlled adult clinical trials, withdrawals due to gastrointestinal adverse reactions, occurred in 4.3% of VICTOZA®-treated patients and 0.5% of placebo-treated patients. Withdrawal due to gastrointestinal adverse events mainly occurred during the first 2-3 months of the trials.

Injection site reactions

Injection site reactions (e.g., injection site rash, erythema) were reported in approximately 2% of VICTOZA®-treated adult patients in the five double-blind, glycemic control trials of at least 26 weeks duration. Less than 0.2% of VICTOZA®-treated patients discontinued due to injection site reactions.

Hypoglycemia

In 5 adult glycemic control, placebo-controlled clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 8 VICTOZA®-treated patients (7.5 events per 100 patient-years). Of these 8 VICTOZA®-treated patients, 7 patients were concomitantly using a sulfonylurea.

In the LEADER trial (see Clinical Studies (14.3)), the incidence of cholelithiasis was 0.3% in both VICTOZA®-treated and placebo-treated patients. The incidence of cholesterol gallstones was 0.2% in both VICTOZA®-treated and placebo-treated patients.

In the LEADER trial (see Clinical Studies (14.3)), the incidence of cholelithiasis was 0.3% (3.9 cases per 1000 patient years of observation) in adult VICTOZA®-treated and 1.1% (2.8 cases per 1000 patient years of observation) in placebo-treated patients, both on a background of standard of care. The incidence of acute cholecystitis was 1.1% (0.9 cases per 1000 patient years of observation) in adult VICTOZA®-treated and 0.7% (1.5 cases per 1000 patient years of observation) in placebo-treated patients. The majority of events required hospitalization or cholecystectomy.

Vital signs

VICTOZA® did not have adverse effects on blood pressure. Mean increases from baseline in heart rate of 2 to 3 beats per minute have been observed in adult patients treated with VICTOZA® compared to placebo.

6.2 Postmarketing Experience

The following additional adverse reactions have been reported during post-approval use of VICTOZA®. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Gastrointestinal: Acute pancreatitis, hemorrhagic and necrotizing pancreatitis sometimes resulting in death, ileus
- General Disorders and Administration Site Conditions: Allergic reactions: rash and pruritus
- Hepatobiliary: Elevations of liver enzymes, hyperbilirubinemia, cholestasis, cholecystitis, cholelithiasis requiring cholecystectomy, hepatitis
- Immune system: Angioedema and anaphylactic reactions
- Metabolism and nutrition: Dehydration resulting from nausea, vomiting and diarrhea
- Neoplasms: Medullary thyroid carcinoma
- Nervous system: Dysgeusia, dizziness
- Renal and urinary: Increased serum creatinine, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis
- Skin and subcutaneous tissue: Cutaneous amyloidosis

7 DRUG INTERACTIONS

7.1 Effects of Delayed Gastric Emptying on Oral Medications

VICTOZA® causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials, VICTOZA® did not affect the absorption of the tested orally administered medications to any clinically relevant degree (see Clinical Pharmacology (12.3)). Nonetheless, caution should be exercised when oral medications are concomitantly administered with VICTOZA®.

7.2 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylureas) or with Insulin

VICTOZA® stimulates insulin release in the presence of elevated blood glucose concentrations. Patients receiving VICTOZA® in combination with an insulin secretagogue (e.g., sulfonylureas) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia. When initiating VICTOZA®, consider reducing the dose of concomitantly administered insulin secretagogues (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia (see Warnings and Precautions (5.4) and Adverse Reactions (6.1)).
8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on animal reproduction studies, there may be risks to the fetus from exposure to VICTOZA® during pregnancy. VICTOZA® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal reproduction studies identified increased adverse developmental outcomes from exposure during pregnancy. Liraglutide exposure was associated with early embryonic deaths and an imbalance in some fetal abnormalities in pregnant rats administered liraglutide during organogenesis at doses that approximate clinical exposures at the maximum recommended human dose (MRHD) of 1.8 mg/day. In pregnant rabbits administered liraglutide during organogenesis, decreased fetal weight and an increased incidence of major fetal abnormalities were seen at exposures below the human exposures at the MRHD [see Animal Data].

The estimated background risk of major birth defects for women with uncontrolled pre-gestational diabetes (Hemoglobin A1c >10) ranges from 6% to 10%. The major birth defect rate has been reported to be as high as 20 to 25% in women with a Hemoglobin A1c >10. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoadiposis, pre-eclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity.

Animal Data

Female rats given subcutaneous doses of 0.1, 0.25 and 1.0 mg/kg/day liraglutide beginning 2 weeks before mating through gestation day 17 had estimated systemic exposures 0.8- 3.5 and 11-times the human exposure at the MRHD based on plasma AUC comparison. The number of early embryonic deaths in the 1 mg/kg/day group increased slightly. Fetal abnormalities and variations in kidneys and blood vessels, irregular ossification of the skull, and a more complete state of ossification occurred at all doses. Median litter size and minimally-kinked ribs occurred at the highest dose. The incidence of fetal malformations in liraglutide-treated groups exceeding concurrent and historical controls were misshapen offspring and/or narrowed opening in larynx at 0.1 mg/kg/day and umbilical hernia at 0.1 and 0.25 mg/kg/day.

Pregnant rabbits given subcutaneous doses of 0.01, 0.025 and 0.05 mg/kg/day liraglutide from gestation day 6 through day 16 inclusive, had estimated systemic exposures less than the human exposure at the MRHD of 1.8 mg/day at all doses, based on plasma AUC. Liraglutide decreased fetal weight and dose-dependently increased the incidence of total major fetal abnormalities at all doses. The incidence of malformations exceeded concurrent and historical controls at 0.01 mg/kg/day (kidneys, scapula), > 0.01 mg/kg/day (eyes, forelimb), 0.025 mg/kg/day (brain, tail and sacral vertebrae, major blood vessels and heart, umbilicus), > 0.025 mg/kg/day (sternum) and at 0.05 mg/kg/day (patal bones, major blood vessels). Irregular ossification and/or skeletal abnormalities occurred in the skull and jaw, vertebrae and ribs, sternum, pelvis, tail, and scapula; and dose-dependent minor skeletal variations were observed. Visceral abnormalities occurred in blood vessels, lungs, liver, and esophagus. Bilobed or bifurcated gallbladder was seen in all treatment groups, but not in the control group.

In pregnant female rats given subcutaneous doses of 0.1, 0.25 and 1.0 mg/kg/day liraglutide from gestation day 6 through weaning or termination of nursing on lactation day 24, estimated systemic exposures were 0.8-3.5 and 11-times human exposure at the MRHD of 1.8 mg/day, based on plasma AUC. A slight delay in parturition was observed in the majority of treated rats. Group mean body weight of neonatal rats from liraglutide-treated dams was lower than neonatal rats from control group dams. Bloody scabs and agitated behavior occurred in male rats descended from dams treated with 1 mg/kg/day liraglutide. Group mean body weight from birth to postpartum day 14 trended lower in F1 offspring of liraglutide-treated dams compared to controls. The incidence of skeletal malformations in neonatal rats from liraglutide-treated dams was lower than neonatal rats from control group dams. Visceral abnormalities occurred in blood vessels, lungs, liver, and esophagus. Bilobed or bifurcated gallbladder was seen in all treatment groups, but not in the control group.

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8.2 Lactation

Risk Summary

There are no data on the presence of VICTOZA® in human milk, the effects on the breastfed infant, or the effects on milk production. Liraglutide was present in milk of lactating rats [see Data]. Developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for VICTOZA® and any potential adverse effects on the breastfed infant from VICTOZA® or from the underlying maternal condition.

Data

In lactating rats, VICTOZA® was present unchanged in milk at concentrations approximately 50% of maternal plasma concentrations.

8.4 Pediatric Use

The safety and effectiveness of VICTOZA® as an adjunct to diet and exercise to improve glycemic control in type 2 diabetes mellitus have been established in pediatric patients 10 years of age and older. Use of VICTOZA® for this indication is supported by a 26-week placebo-controlled clinical trial and a 26-week open-label extension in 134 pediatric patients 10 to 17 years of age with type 2 diabetes mellitus, a pediatric pharmacokinetic study, and studies in adults with type 2 diabetes mellitus [see Clinical Pharmacology (12.3) and Clinical Studies (14.1,14.2)]. The risk of hypoglycemia was higher with VICTOZA® in pediatric patients regardless of insulin and/or metformin use [see Adverse Reactions (6.1)].

The safety and effectiveness of VICTOZA® have not been established in pediatric patients less than 10 years of age.

8.5 Geriatric Use

In the VICTOZA® treatment arms of the glycemic control trials, a total of 852 (19.3%) of the patients were 74 years of age and 145 (3.4%) were 75 years of age and over [see Clinical Studies (14.1)]. In the VICTOZA® treatment arm of the LEADER trial [see Clinical Studies (14.3)], a total of 1738 (37.2%) patients were 65 to 74 years of age, 401 (8.6%) were 75 to 84 years of age, and 17 (0.4%) were 85 years of age or older at baseline. No overall differences in safety or effectiveness for VICTOZA® have been observed between patients 65 years of age and older and younger patients.
VICTOZA® (liraglutide) injection 1.2 mg, 1.8 mg-treated patients. Patients who did not change the overall exposure (AUC) of griseofulvin following co-administration of a single dose of griseofulvin 500 mg at steady state. Acetaminophen 1000 mg, administered 8 hours after the dose of VICTOZA® at steady state. Atorvastatin Cmax was decreased by 38% and median Tmax was decreased from 1 h to 3 h with VICTOZA®. Acetaminophen VICTOZA® did not change the overall exposure (AUC) of acetaminophen following a single dose of acetaminophen 1000 mg, administered 8 hours after the dose of VICTOZA® at steady state. Acetaminophen Cmax was decreased by 31% and median Tmax was delayed up to 15 minutes.

Griseofulvin VICTOZA® did not change the overall exposure (AUC) of griseofulvin following co-administration of a single dose of griseofulvin 500 mg with VICTOZA® at steady state. Griseofulvin Cmax increased by 37% while median Tmax changed.

Oral Contraceptives A single dose of an oral contraceptive combination product containing 0.03 mg ethinylestradiol and 0.15 mg levonorgestrel was administered under fed conditions and 7 hours after the dose of VICTOZA® at steady state. VICTOZA® lowered ethinylestradiol and levonorgestrel Cmax by 12% and 13%, respectively. There was no effect of VICTOZA® on the overall exposure (AUC) of ethinylestradiol. VICTOZA® increased the levonorgestrel AUC— by 18%. VICTOZA® delayed Tmax for both ethinylestradiol and levonorgestrel by 1.5 h.

Insulin Detemir No pharmacokinetic interaction was observed between VICTOZA® and insulin detemir when separate subcutaneous injections of insulin detemir 0.5 Unit/kg (single-dose) and VICTOZA® 1.8 mg (steady state) were administered in patients with type 2 diabetes mellitus.

12.6 Immunogenicity The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those with VICTOZA® or other liraglutide products.

A subset of VICTOZA®-treated patients (1104 of 2901, 44%) in five adult double-blind clinical trials of 26 weeks duration or longer were tested for the presence of anti-liraglutide antibodies at the end of treatment [see Clinical Studies (14.1)] and 102/1104 (9%) of VICTOZA®-treated patients developed anti-liraglutide antibodies. Of these 102 VICTOZA®-treated patients, 56 (5%) patients developed antibodies that cross-reacted with native GLP-1. These cross-reacting antibodies were not tested for neutralizing effect against native GLP-1, and thus the potential for clinically significant neutralization of native GLP-1 was not assessed. Antibodies that had a neutralizing effect on liraglutide in an in vitro assay occurred in 12 (1%) of the VICTOZA®-treated patients. There was no identified clinically significant effect of anti-liraglutide antibodies on effectiveness of VICTOZA®.

In five double-blind adult glycemic control trials of VICTOZA®, events from a composite of adverse events potentially related to immunogenicity (e.g., urticaria, angioedema) occurred among 0.8% of VICTOZA®-treated patients and among 0.4% of comparator-treated patients. Urticaria accounted for approximately one-half of the events in this composite for VICTOZA®-treated patients. Patients who developed anti-liraglutide antibodies were not more likely to develop events from the immunogenicity events composite than were patients who did not develop anti-liraglutide antibodies.

In the LEADER trial [see Clinical Studies (14.3)], anti-liraglutide antibodies were detected in 11 out of the 1247 (0.9%) adult VICTOZA®-treated patients with antibody measurements. Of the 11 adult VICTOZA®-treated patients who developed anti-liraglutide antibodies, none were observed to develop neutralizing antibodies to liraglutide, and 5 patients (0.4%) developed cross-reacting antibodies against native GLP-1.

In a clinical trial with pediatric patients aged 10 years and older [see Clinical Studies (14.2)], anti-liraglutide antibodies were detected in 1 (2%) VICTOZA®-treated patient at week 26 and 5 (9%) VICTOZA®-treated patients at week 53. None of the 5 patients had antibodies cross reactive to native GLP-1 or had neutralizing antibodies.
13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

A 1-week carcinogenicity study was conducted in male and female CD-1 mice at doses of 0.03, 0.2, 1.0, and 3.0 mg/kg/day liraglutide administered by bolus subcutaneous injection yielding systemic exposures 0.2-, 2-, 10- and 45-times the human exposure, respectively, at the MRHD of 1.8 mg/day based on plasma AUC comparison. A dose-related increase in benign thyroid C-cell adenomas was seen in the 1.0 and the 3.0 mg/kg/day groups with incidences of 13% and 19% in males and 6% and 20% in females, respectively. C-cell adenomas did not occur in control groups or 0.03 and 0.2 mg/kg/day groups. Treatment-related malignant C-cell carcinomas occurred in 3% of females in the 3.0 mg/kg/day group. Thyroid C-cell tumors are rare findings during carcinogenicity testing in mice. A treatment-related increase in thyroid C-cell tumors was also studied in a cardiovascular outcomes trial (LEADER trial).

In this 26-week trial, 1,091 adult patients with type 2 diabetes mellitus who were randomized to liraglutide (VICTOZA® 0.6 mg, VICTOZA® 1.2 mg, or glimepiride 8 mg) were included. The primary endpoint was a composite of cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke over 26 weeks. The secondary endpoints included the change from baseline HbA1c and fasting plasma glucose (FPG) levels.

Table 3 Results of a 52-week Monotherapy Trial in Adults with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>Drug</th>
<th>HbA1c (%)</th>
<th>Mean HbA1c (%)</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>VICTOZA® 1.2 mg</td>
<td>8.2</td>
<td>-20**</td>
<td>-0.6</td>
</tr>
<tr>
<td>VICTOZA® 1.8 mg</td>
<td>8.2</td>
<td>-21**</td>
<td>-0.7</td>
</tr>
<tr>
<td>Glimepiride 8 mg</td>
<td>8.2</td>
<td>-20**</td>
<td>-0.6</td>
</tr>
</tbody>
</table>

*p-value < 0.05
**p-value < 0.001

In this 52-week trial, 746 adult patients with type 2 diabetes mellitus were randomized to VICTOZA® 1.2 mg, VICTOZA® 1.8 mg, or glimepiride 8 mg. Patients who were randomized to glimepiride were initially treated with 0.2 mg daily for 2 weeks, increasing to 4 mg daily for another two weeks, and finally increasing to 8 mg daily. Treatment with VICTOZA® 1.2 mg and 1.8 mg resulted in a statistically significant reduction in HbA1c compared to glimepiride (Table 3). The percentage of patients who discontinued due to ineffective therapy was 3.6% in the VICTOZA® 1.8 mg treatment group, 6.0% in the VICTOZA® 1.2 mg treatment group, and 10.1% in the glimepiride-treatment group.

The mean age of participants was 53 years, and the mean duration of diabetes was 5 years. Participants were 49.7% male, 77.5% White, 12.6% Black or African American and 35.0% of Hispanic or Latino ethnicity. The mean BMI was 33.1 kg/m².
Table 4 Results of a 26-week Trial of VICTOZA<sup>®</sup> as Add-on to Metformin in Adults with Type 2 Diabetes Mellitus<sup>a</sup>

<table>
<thead>
<tr>
<th></th>
<th>VICTOZA&lt;sup&gt;®&lt;/sup&gt; 1.8 mg + Metformin</th>
<th>VICTOZA&lt;sup&gt;®&lt;/sup&gt; 1.2 mg + Metformin</th>
<th>Placebo + Metformin</th>
<th>Glimepiride 4 mg + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treatment Population (N)</td>
<td>242</td>
<td>240</td>
<td>121</td>
<td>242</td>
</tr>
<tr>
<td>HbA1c (%) (Mean)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-1.0</td>
<td>-1.0</td>
<td>-0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.5, -0.5)</td>
<td>(-1.5, -0.5)</td>
<td>(-0.6, 0.3)</td>
<td></td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c&lt;sup&gt;c&lt;/sup&gt; &lt;7%</td>
<td>40</td>
<td>35</td>
<td>11</td>
<td>36</td>
</tr>
</tbody>
</table>

Fasting Plasma Glucose (mg/dL) (Mean)

<table>
<thead>
<tr>
<th></th>
<th>(Baseline)</th>
<th>Change from baseline (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>95% Confidence Interval</th>
<th>Percentage of patients achieving HbA1c&lt;sup&gt;c&lt;/sup&gt; &lt;7%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>88.0</td>
<td>-2.8</td>
<td>(-4.2, -1.4)</td>
<td>48</td>
</tr>
<tr>
<td>Difference from placebo + metformin arm (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-1.3</td>
<td>-2.0</td>
<td>(-3.5, -0.7)</td>
<td>54</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-3.7, -0.7)</td>
<td>(-3.7, -0.7)</td>
<td>(-4.3, -0.1)</td>
<td></td>
</tr>
</tbody>
</table>

Table 5 Results of a 26-week Open-label Trial of VICTOZA<sup>®</sup> Compared to Sitagliptin (both in combination with metformin) in Adults with Type 2 Diabetes Mellitus<sup>a</sup>

<table>
<thead>
<tr>
<th></th>
<th>VICTOZA&lt;sup&gt;®&lt;/sup&gt; 1.8 mg + Metformin</th>
<th>VICTOZA&lt;sup&gt;®&lt;/sup&gt; 1.2 mg + Metformin</th>
<th>Sitagliptin 100 mg + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treatment Population (N)</td>
<td>162</td>
<td>157</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%) (Mean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-1.2</td>
<td>-1.0</td>
<td>-1.1**</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.4, -0.9)</td>
<td>(-1.4, -0.9)</td>
<td>(-1.4, -0.9)</td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c&lt;sup&gt;c&lt;/sup&gt; &lt;7%</td>
<td>42</td>
<td>35</td>
<td>11</td>
</tr>
</tbody>
</table>

Fasting Plasma Glucose (mg/dL) (Mean)

<table>
<thead>
<tr>
<th></th>
<th>(Baseline)</th>
<th>Change from baseline (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>95% Confidence Interval</th>
<th>Percentage of patients achieving HbA1c&lt;sup&gt;c&lt;/sup&gt; &lt;7%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>86.5</td>
<td>-2.6</td>
<td>(-3.2, -2.0)</td>
<td>40</td>
</tr>
<tr>
<td>Difference from placebo + metformin arm (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-1.2</td>
<td>-1.6</td>
<td>(-2.7, -0.2)</td>
<td>45</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-2.4, -0.2)</td>
<td>(-2.4, -0.2)</td>
<td>(-2.6, -0.0)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Intent-to-treatment population using last observation on study
<sup>b</sup>Least squares mean adjusted for baseline value
<sup>c</sup>IVctora® Compared to Sitagliptin. Both as Add-on to Metformin

In this 26-week, open-label trial, 665 adult patients with type 2 diabetes mellitus on a background of metformin ≥1,500 mg per day were randomized to VICTOZA® 1.2 mg once daily, VICTOZA® 1.8 mg once daily or sitagliptin 100 mg once daily, all dosed according to approved labeling. Patients were to continue their current treatment on metformin at a stable, pre-trial dose level and dosing frequency.

The mean age of participants was 56 years, and the mean duration of diabetes was 6 years. Participants were 52.9% male, 86.6% White, 7.2% Black or African American and 16.2% of Hispanic or Latino ethnicity. The mean BMI was 29.8 kg/m².

The primary endpoint was the change in HbA1c from baseline to Week 26. Treatment with VICTOZA® 1.2 mg and VICTOZA® 1.8 mg resulted in statistically significant reductions in HbA1c relative to sitagliptin 100 mg (Table 5). The percentage of patients who discontinued due to ineffective therapy was 3.1% in the group randomized to continued treatment with VICTOZA® 1.8 mg, 3.5% for VICTOZA® 1.2 mg and metformin and 1.8% in the group randomized to add-on treatment with VICTOZA® 1.8 mg and metformin alone.

<sup>Table 6 Results of a 26-week Open-label Trial of Insulin detemir as add-on to VICTOZA® + Metformin Compared to Continued Treatment with VICTOZA® + Metformin alone in Adult Patients with Type 2 Diabetes Mellitus not Achieving HbA1c <7% after 12 weeks of Metformin and VICTOZA®<sup>b</sup><sup>c</sup></sup>

<table>
<thead>
<tr>
<th></th>
<th>Baseline (week 0)</th>
<th>Change from baseline (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>95% Confidence Interval</th>
<th>Percentage of patients achieving HbA1c&lt;sup&gt;c&lt;/sup&gt; &lt;7%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>88.0</td>
<td>-2.5</td>
<td>(-3.4, -1.6)</td>
<td>48</td>
</tr>
<tr>
<td>Difference from VICTOZA® + metformin arm (LS mean)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-1.5</td>
<td>-2.0</td>
<td>(-3.0, -1.0)</td>
<td>53</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-2.4, -0.6)</td>
<td>(-2.4, -0.6)</td>
<td>(-2.6, -0.4)</td>
<td></td>
</tr>
</tbody>
</table>

Mean HbA1c (%)

<table>
<thead>
<tr>
<th></th>
<th>Mean HbA1c (%) (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>7.8 (7.5-8.0)</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-0.5 (0.0-1.0)</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.2, -0.4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Intent-to-treatment population using last observation on study
<sup>b</sup>Least squares mean adjusted for baseline value
<sup>c</sup>IVctora® Compared to Sitagliptin. Both as Add-on to Metformin

Add-on to Sulfonylurea

In this 26-week trial, 1,041 adult patients with type 2 diabetes mellitus were randomized to VICTOZA® 0.6 mg, VICTOZA® 1.2 mg, VICTOZA® 1.8 mg, placebo, or rosiglitazone 4 mg (one-half of the maximal approved dose in the United States), all as add-on to glimepiride. Randomization occurred after a 4-week run-in period consisting of an initial, 2-week, forced-glimepiride titration period followed by a maintenance period of another 2 weeks. During the titration period, doses of glimepiride were increased to 4 mg/day. The doses of glimepiride could be reduced (at the discretion of the investigator) from 4 mg/day to 3 mg/day or 2 mg/day (minimum) after randomization, in the event of unacceptable hypoglycemia or other adverse events.

The mean age of participants was 56 years, and the mean duration of diabetes was 8 years. Participants were 55.7% male, 91.3% White, 5.6% Black or African American and 12.5% of Hispanic or Latino ethnicity. The mean BMI was 23.0 kg/m².

The primary endpoint of the study was the change in HbA1c from baseline to Week 26. Treatment with VICTOZA® 1.2 mg and VICTOZA® 1.8 mg resulted in a statistically significant reduction in mean HbA1c compared to placebo add-on to glimepiride (Table 7). The percentage of patients who discontinued due to ineffective therapy was 3.0% in the VICTOZA® 1.8 mg group, equivalent to the percentage of patients who discontinued in the VICTOZA® 1.2 mg group.
Table 7 Results of a 26-week Trial of VICTOZA® as add-on to Sulfonylurea in Adult Patients with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>HbA1c (%) (Mean)</th>
<th>VICTOZA® 1.8 mg + Metformin</th>
<th>Placebo + Metformin</th>
<th>Rosiglitazone 4 mg + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Population (N)</td>
<td>294</td>
<td>228</td>
<td>114</td>
</tr>
<tr>
<td>Body Weight (kg) (Mean)</td>
<td>85</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>Baseline</td>
<td>85.1</td>
<td>85.1</td>
<td>85.1</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.1</td>
<td>-1.1</td>
<td>-1.1</td>
</tr>
<tr>
<td>Difference from placebo + glimepiride arm (adjusted mean)</td>
<td>-1.4**</td>
<td>-1.3*</td>
<td>-1.3**</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.6, -1.1)</td>
<td>(-1.5, -1.1)</td>
<td>(-1.5, -1.1)</td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c &lt;7%</td>
<td>42</td>
<td>35</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 8 Results of a 26-week Trial of VICTOZA® as Add-on to Metformin and Sulfonylurea in Adult Patients with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>VICTOZA® 1.8 mg + Metformin</th>
<th>Placebo + Metformin</th>
<th>Insulin glargine® + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Population (N)</td>
<td>230</td>
<td>114</td>
</tr>
<tr>
<td>Body Weight (kg) (Mean)</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>Baseline</td>
<td>85.1</td>
<td>85.1</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.1</td>
<td>-1.1</td>
</tr>
<tr>
<td>Difference from placebo + glimepiride arm (adjusted mean)</td>
<td>-1.4**</td>
<td>-1.3*</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.6, -1.1)</td>
<td>(-1.5, -1.1)</td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c &lt;7%</td>
<td>53</td>
<td>51</td>
</tr>
</tbody>
</table>

Table 9 Results of a 26-week Trial of VICTOZA® vs. Exenatide in Adult Patients with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th>VICTOZA® 1.8 mg once daily + metformin and/or sulfonylurea</th>
<th>Exenatide 10 mcg twice daily + metformin and/or sulfonylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Population (N)</td>
<td>233</td>
</tr>
<tr>
<td>HbA1c (%) (Mean)</td>
<td>8.2</td>
</tr>
<tr>
<td>Baseline</td>
<td>8.3</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.1</td>
</tr>
<tr>
<td>Difference from exenatide arm (adjusted mean)</td>
<td>-0.3**</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-0.53, -0.27)</td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c &lt;7%</td>
<td>54</td>
</tr>
</tbody>
</table>

Table 10 Results of a 26-week Trial of VICTOZA® as Add-on to Metformin and Thiazolidinediones in Adult Patients with Type 2 Diabetes Mellitus

VICTOZA® Compared to Exenatide, Both as Add-on to Metformin and/or Sulfonylurea Therapy

In this 26-week, open-label trial, 464 adult patients with type 2 diabetes mellitus on a background of metformin monotherapy, sulfonylurea monotherapy or a combination of metformin and sulfonylurea were randomized to VICTOZA® 1.8 mg or exenatide 10 mcg twice daily. Maximal tolerated doses of background therapy were to remain unchanged for the duration of the trial. Patients randomized to exenatide started on a dose of 5 mcg twice-daily for 4 weeks and then were escalated to 10 mcg twice daily.

The mean age of participants was 57 years, and the mean duration of diabetes was 8 years. Participants were 51.9% male, 91.8% White, 5.4% Black or African American and 12.3% of Hispanic or Latino ethnicity. The mean BMI was 32.9 kg/m².

Treatment with VICTOZA® 1.8 mg resulted in statistically significant reductions in HbA1c and FPG relative to exenatide (Table 9). The percentage of patients who discontinued due to ineffective therapy was 0.4% in the VICTOZA® treatment group and 0% in the exenatide treatment group. Both treatment groups had a mean decrease from baseline in body weight of approximately 3 kg.

Add-on to Metformin and Sulfonylurea

In this 26-week trial, 581 adult patients with type 2 diabetes mellitus were randomized to VICTOZA® 1.8 mg, placebo, or insulin glargine, all as add-on to metformin and glimepiride. Randomization took place after a 6-week run-in period consisting of a 3-week forced metformin and glimepiride titration period followed by a maintenance period of another 3 weeks. During the titration period, doses of metformin and glimepiride were increased up to 2,000 mg/d/day and 4 mg/day, respectively. After randomization, patients randomized to VICTOZA® 1.8 mg underwent a 2-week period of titration with VICTOZA®. During the trial, the VICTOZA® and metformin doses were fixed, although glimepiride and insulin glargine doses could be adjusted. Patients titrated glargine twice-weekly during the first 8 weeks of treatment based on self-measured fasting plasma glucose on the day of titration. After Week 8, the frequency of insulin glargine titration was left to the discretion of the investigator, but, at a minimum, the glargine dose was to be revised, if necessary, at Weeks 12 and 18. Only 20% of glargine-treated patients achieved the pre-specified target fasting plasma glucose of ≤100 mg/dL. Therefore, optimal titration of glargine was not achieved for 80% of patients.**p-value <0.0001

Add-on to Metformin and Thiazolidinediones

In this 26-week trial, 533 adult patients with type 2 diabetes mellitus were randomized to VICTOZA® 1.2 mg, VICTOZA® 1.8 mg or placebo, all as add-on to rosiglitazone (8 mg) plus metformin (2,000 mg). Patients underwent a 9 week run-in period (3-week forced dose escalation followed by a 6-week maintenance phase) with rosiglitazone (starting at 4 mg and increasing to 8 mg/day within 2 weeks) and metformin (starting at 500 mg with increasing weekly increments of 500 mg to a final dose of 2,000 mg/day). Only patients who tolerated the final dose of rosiglitazone (8 mg/day) and metformin (2,000 mg/day) and completed the 6-week dose maintenance phase were eligible for randomization into the trial.

The mean age of participants was 55 years, and the mean duration of diabetes was 9 years. Participants were 61.6% male, 84.2% White, 10.2% Black or African American and 16.4% of Hispanic or Latino ethnicity. The mean BMI was 33.9 kg/m².

Treatment with VICTOZA® as add-on to metformin and rosiglitazone produced a statistically significant reduction in mean HbA1c compared to placebo add-on to metformin and rosiglitazone (Table 10). The percentage of patients who discontinued due to ineffective therapy was 1.7% in the VICTOZA® 1.8 mg + metformin + rosiglitazone treatment group, 1.7% in the VICTOZA® 1.2 mg + metformin + rosiglitazone treatment group, and 16.4% in the placebo + metformin + rosiglitazone treatment group.

Add-on to Metformin and Thiazolidinediones

In this 26-week trial, 533 adult patients with type 2 diabetes mellitus were randomized to VICTOZA® 1.2 mg, VICTOZA® 1.8 mg or placebo, all as add-on to rosiglitazone (8 mg) plus metformin (2,000 mg). Patients underwent a 9 week run-in period (3-week forced dose escalation followed by a 6-week maintenance phase) with rosiglitazone (starting at 4 mg and increasing to 8 mg/day within 2 weeks) and metformin (starting at 500 mg with increasing weekly increments of 500 mg to a final dose of 2,000 mg/day). Only patients who tolerated the final dose of rosiglitazone (8 mg/day) and metformin (2,000 mg/day) and completed the 6-week dose maintenance phase were eligible for randomization into the trial.

The mean age of participants was 55 years, and the mean duration of diabetes was 9 years. Participants were 61.6% male, 84.2% White, 10.2% Black or African American and 16.4% of Hispanic or Latino ethnicity. The mean BMI was 33.9 kg/m².

Treatment with VICTOZA® as add-on to metformin and rosiglitazone produced a statistically significant reduction in mean HbA1c compared to placebo add-on to metformin and rosiglitazone (Table 10). The percentage of patients who discontinued due to ineffective therapy was 1.7% in the VICTOZA® 1.8 mg + metformin + rosiglitazone treatment group, 1.7% in the VICTOZA® 1.2 mg + metformin + rosiglitazone treatment group, and 16.4% in the placebo + metformin + rosiglitazone treatment group.
VICTOZA® Compared to Placebo Both With or Without metformin and/or Sulfonylurea and/or Pioglitazone and/or Basal or Premix insulin in Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment

In this 26-week, double-blind, randomized, placebo-controlled, parallel-group trial in adult patients with type 2 diabetes mellitus, 279 patients with moderate renal impairment, as per MDRD formula (eGFR 30–59 mL/min/1.73 m²), were randomized to VICTOZA® or placebo once daily. VICTOZA® was added to the patient’s stable pre-trial antibiotic regimen (insulin therapy and/or metformin, pioglitazone, or sulfonylurea). The dose of VICTOZA® was escalated according to approved labeling to achieve a dose of 1.8 mg per day. The insulin dose was reduced by 20% at randomization for patients with baseline HbA₁c ≤ 8% and fixed until liraglutide dose escalation was complete. Dose reduction of insulin and SU was allowed in case of hypoglycemia, up titration of insulin was allowed but not beyond the pre-trial dose.

The mean age of participants was 67 years, and the mean duration of diabetes was 15 years. Participants were 50.5% male, 92.3% White, 6.6% Black or African American, and 7.2% of Hispanic or Latino ethnicity. The mean BMI was 33.9 kg/m². Approximately half of patients had an eGFR between 30 and <45 mL/min/1.73 m².

Treatment with VICTOZA® resulted in a statistically significant reduction in HbA₁c from baseline at Week 26 compared to placebo (see Table 11). 123 patients reached the 1.8 mg dose of VICTOZA®.

### Table 11 Results of a 26-week Trial of VICTOZA® Compared to Placebo in Adult Patients with Type 2 Diabetes Mellitus and Moderate Renal Impairment

<table>
<thead>
<tr>
<th></th>
<th>VICTOZA® 1.8 mg + insulin and/or OAD</th>
<th>Placebo + insulin and/or OAD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA₁c (%)</strong></td>
<td>Baseline</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>Change from baseline (estimated mean)</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>Difference from placebo</td>
<td>-0.6*</td>
</tr>
<tr>
<td></td>
<td>95% Confidence Interval</td>
<td>(-0.8, -0.3)</td>
</tr>
<tr>
<td><strong>Proportion achieving HbA₁c &lt; 7%</strong></td>
<td>Baseline</td>
<td>39.3</td>
</tr>
<tr>
<td></td>
<td>Change from baseline (estimated mean)</td>
<td>-22</td>
</tr>
<tr>
<td></td>
<td>Difference from placebo</td>
<td>-12**</td>
</tr>
<tr>
<td></td>
<td>95% Confidence Interval</td>
<td>(-23, -0.8)</td>
</tr>
<tr>
<td><strong>FPG (mg/dL)</strong></td>
<td>Baseline</td>
<td>171</td>
</tr>
<tr>
<td></td>
<td>Change from baseline (estimated mean)</td>
<td>-22</td>
</tr>
<tr>
<td></td>
<td>Difference from placebo</td>
<td>-12**</td>
</tr>
<tr>
<td></td>
<td>95% Confidence Interval</td>
<td>(-23, -0.8)</td>
</tr>
</tbody>
</table>

*The change from baseline at end of treatment to HbA₁c and FPG was analyzed using a pattern mixture model with multiple imputation. Missing observations (10.6% in the VICTOZA® 14.5% in the placebo) were imputed from the placebo arm based on multiple (n=10,000) imputations. The data for week 26 was then analyzed with an ANCOVA model containing treatment, sex and age group as fixed effects and baseline value as covariate.

**Categories are derived from continuous measurements of HbA₁c using a pattern mixture model with multiple imputation for missing observations.

### Table 12 Results at week 26 in a trial comparing VICTOZA® in combination with metformin with or without basal insulin versus Placebo in combination with metformin with or without basal insulin in Pediatric Patients Aged 10 Years and Older with Type 2 Diabetes Mellitus

<table>
<thead>
<tr>
<th></th>
<th>VICTOZA®+metformin+basal insulin</th>
<th>Placebo+metformin+basal insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>68</td>
<td>68</td>
</tr>
<tr>
<td><strong>HbA₁c (%)</strong></td>
<td>Baseline</td>
<td>7.9</td>
</tr>
<tr>
<td></td>
<td>Adjusted end mean change from baseline after 26 weeks</td>
<td>-0.64</td>
</tr>
<tr>
<td></td>
<td>Treatment difference (95% CI)</td>
<td>-1.06 [-1.65, -0.46]</td>
</tr>
<tr>
<td><strong>Percentage of patients achieving HbA₁c &lt; 7%</strong></td>
<td>Baseline</td>
<td>63.7</td>
</tr>
<tr>
<td></td>
<td>Adjusted end mean change from baseline after 26 weeks</td>
<td>-19.4</td>
</tr>
<tr>
<td></td>
<td>Treatment difference (95% CI)</td>
<td>-19.4 [-23, -0.8]</td>
</tr>
</tbody>
</table>

*The change from baseline at end of treatment in HbA₁c and FPG was analyzed using a pattern mixture model with multiple imputation. Missing observations (10.6% in the VICTOZA® 14.5% in the placebo) were imputed from the placebo arm based on multiple (n=10,000) imputations. The data for week 26 was then analyzed with an ANCOVA model containing treatment, sex and age group as fixed effects and baseline value as covariate.

**Categories are derived from continuous measurements of HbA₁c using a pattern mixture model with multiple imputation for missing observations.

### 14.2 Glycemic Control Trial in Pediatric Patients Aged 10 Years and Older with Type 2 Diabetes Mellitus

VICTOZA® was evaluated in a 26-week, double-blind, randomized, parallel group, placebo controlled multi-center trial (NCT01541215), in 134 pediatric patients with type 2 diabetes mellitus aged 10 years and older. Patients were randomized to VICTOZA® once-daily or placebo once-daily in combination with metformin with or without basal insulin treatment. All patients were on a metformin dose of 1000 to 2000 mg prior to randomization. The basal insulin dose was decreased by 20% at randomization and VICTOZA® was titrated weekly by 0.6 mg for 2 to 3 weeks based on tolerability and a average fasting plasma glucose goal of ≤110 mg/dL.

The mean age was 14.6 years: 29.9% were ages 10-14 years, and 70.1% were greater than 14 years of age. 50.5% male, 92.3% White, 6.6% Black or African American, and 7.2% of Hispanic or Latino ethnicity. The mean BMI was 33.9 kg/m². Approximately half of patients had an eGFR between 30 and <45 mL/min/1.73 m².

### 14.3 Cardiovascular Outcomes Trial in Adult Patients with Type 2 Diabetes Mellitus and Atherosclerotic Cardiovascular Disease

The LEADER trial (NCT01179048) was a multi-national, multi-center, placebo-controlled, double-blind trial. In this study, 9,240 adult patients with inadequately controlled type 2 diabetes mellitus and atherosclerotic cardiovascular disease (CVD) were randomized to VICTOZA® 1.8 mg or placebo for a median duration of 3.5 years. The study compared the risk of major adverse cardiovascular events between VICTOZA® and placebo when these were added to, and used concurrently with, background standard of care treatments for type 2 diabetes mellitus. The primary endpoint, major adverse cardiac events (MACE), was the time to first occurrence of a three part composite outcome which included: cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

Patients eligible to enter the trial were: 50 years of age or older and had established, stable, cardiovascular, cerebrovascular, peripheral artery disease, chronic kidney disease or New York Heart Association (NYHA) class II or III heart failure (80% of the enrolled population) or were 60 years of age or older and had other specified risk factors for cardiovascular disease (20% of the enrolled population).

At baseline, demographic and disease characteristics were balanced. The mean age was 64 years and the population was 64.3% male, 77.5% White, 10.0% Asian, and 8.3% Black or African American. In the study, 12.1% of the population identified as Hispanic or Latino ethnicity. The mean duration of type 2 diabetes mellitus was 12.8 years, the mean HbA₁c was 8.7% and the mean BMI was 32.5 kg/m². A history of previous myocardial infarction was reported in 31% of randomized individuals, a prior revascularization procedure in 39%, a prior ischemic stroke in 11%, documented symptomatic coronary disease in 9%, documented asymptomatic cardiac ischemia in 26%, and a diagnosis of NYHA class II to III heart failure in 14%. The mean eGFR at baseline was 79 mL/min/1.73 m² and 41.8% of patients had mild renal impairment (eGFR 60 to 90 mL/min/1.73 m²), 20.7% had moderate renal impairment (eGFR 30 to 60 mL/min/1.73 m²) and 2.4% of patients had severe renal impairment (eGFR ≤ 30 mL/min/1.73 m²).

At baseline, patients were treated with their diabetes with; diet and exercise only (3.9%), oral antidiabetic drugs only (51.5%), oral antidiabetic drugs and insulin (36.7%) or insulin only (7.9%). The most common background anti-diabetic drugs used at baseline and in the trial were metformin, sulfonylurea and insulin. Use of DPP-4 inhibitors and other GLP-1 receptor agonists was excluded by protocol and sodium-glucose cotransporter-2 (SGLT-2) inhibitors were either not approved or not widely available. At baseline, cardiovascular disease and risk factors were managed with; non-diuretic antihypertensives (92.4%), beta-blockers (72.1%) and platelet aggregation inhibitors (66.8%). During the trial, investigators could modify anti-diabetic and cardiovascular medications to achieve local standard of care treatment targets with respect to blood glucose, lipid, and blood pressure, and manage patients recovering from an acute coronary syndrome or stroke event per local treatment guidelines.

For the primary analysis, a Cox proportional hazards model was used to test for non-interiority against the pre-specified risk margin of 1.3 for the hazard ratio of MACE and to test for superiority on MACE if non-interiority was demonstrated. Type 1 error was controlled across multiple tests.

VICTOZA® significantly reduced the occurrence of MACE. The estimated hazard ratio (95% CI) for time to first MACE was 0.87 (0.78, 0.97). Refer to Figure 5 and Table 13.

Vital status was available for 99.7% of subjects in the trial. A total of 828 deaths were recorded during the LEADER trial. A majority of the deaths in the trial were categorized as cardiovascular deaths and risk factors for cardiovascular disease (20% of the enrolled population).
Hypersensitivity Reactions
Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of VICTOZA®. Advise patients on the symptoms of hypersensitivity reactions and instruct them to stop taking VICTOZA® and seek medical advice promptly if such symptoms occur (see Warnings and Precautions (5.6)).

Acute Gallbladder Disease
Inform patients of the potential risk for cholelithiasis or cholecystitis. Instruct patients to contact their physician if cholelithiasis or cholecystitis is suspected for appropriate clinical follow-up (see Warnings and Precautions (5.7)).

Missed Dose
Inform patients not to take an extra dose of VICTOZA® to make up for a missed dose. If a dose is missed, the once-daily regimen should be resumed as prescribed with the next scheduled dose. If more than 3 days have elapsed since the last dose, advise the patient to reinitiate VICTOZA® at 0.6 mg to mitigate any gastrointestinal symptoms associated with reinitiation of treatment. VICTOZA® should be titrated at the discretion of the healthcare provider (see Dosage and Administration (2.2)).

Figure 5 Kaplan-Meier: Time to First Occurrence of a MACE in the LEADER Trial
(Patients with Type 2 Diabetes Mellitus and Atherosclerotic CVD)

Table 13 Treatment Effect for the Primary Composite Endpoint, MACE, and its Components in the LEADER Trial (Patients with Type 2 Diabetes Mellitus and Atherosclerotic CVD)\(^a\)

<table>
<thead>
<tr>
<th>Event</th>
<th>VICTOZA® N=4668</th>
<th>Placebo N=4672</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite cardiovascular death, non-fatal myocardial infarction, non-fatal stroke (MACE) (time to first occurrence)(^b)</td>
<td>608 (13.0%)</td>
<td>694 (14.9%)</td>
<td>0.87 (0.78; 0.97)</td>
</tr>
<tr>
<td>Non-fatal myocardial infarction(^b)</td>
<td>281 (6.0%)</td>
<td>317 (6.8%)</td>
<td>0.88 (0.75; 1.00)</td>
</tr>
<tr>
<td>Non-fatal stroke(^b)</td>
<td>159 (3.4%)</td>
<td>177 (3.8%)</td>
<td>0.90 (0.72; 1.11)</td>
</tr>
<tr>
<td>Cardiovascular death(^b)</td>
<td>219 (4.7%)</td>
<td>278 (6%)</td>
<td>0.78 (0.66; 0.93)</td>
</tr>
</tbody>
</table>

\(^a\)Full analysis set (all randomized patients)
\(^b\)Cox-proportional hazards model with treatment as a factor
\(^c\)p-value for superiority (2-sided) 0.011
\(^d\)Number and percentage of first events

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied
VICTOZA® Injection: 18 mg/mL (6 mg/mL) clear, colorless solution in a pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg is available in the following package sizes:
2 x VICTOZA® pen NDC 0169-4060-12
3 x VICTOZA® pen NDC 0169-4060-13

16.2 Recommended Storage
Prior to first use, VICTOZA® should be stored in a refrigerator between 36°F to 46°F (2°C to 8°C). Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze VICTOZA® and do not use VICTOZA® if it has been frozen.

After first use of the VICTOZA® pen, the pen can be stored for 30 days at controlled room temperature (59°F to 86°F; 15°C to 30°C) or in a refrigerator (36°F to 46°F; 2°C to 8°C). Keep the pen cap on when not in use. Protect VICTOZA® from excessive heat and sunlight. Always remove and safely discard the needle after each injection and store the VICTOZA® pen without an injection needle attached. This will reduce the potential for contamination, infection, and leakage while also ensuring dosing accuracy. Always use a new needle for each injection to prevent contamination.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Risk of Thyroid C-cell Tumors
Inform patients that liraglutide causes benign and malignant thyroid C-cell tumors in mice and rats and that the human relevance of this finding is unknown. Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, hoarseness, dysphagia, or dyspnea) to their physician (see Boxed Warning and Warnings and Precautions (5.1)).

Pancreatitis
Inform patients of the potential risk for pancreatitis. Explain that persistent severe abdominal pain that may radiate to the back and which may or may not be accompanied by vomiting, is the hallmark symptom of acute pancreatitis. Instruct patients to discontinue VICTOZA® promptly and contact their physician if persistent severe abdominal pain occurs (see Warnings and Precautions (5.2)).

Never Share a VICTOZA® Pen Between Patients
Advise patients that they must never share a VICTOZA® pen with another person, even if the needle is changed, because doing so caries a risk for transmission of blood-borne pathogens (see Warnings and Precautions (5.3)).

Hypoglycemia
Inform patients that hypoglycemia has been reported when VICTOZA® is used with insulin secretagogues or insulin and may occur in pediatric patients regardless of concomitant antidiabetic treatment. Educate patients or caregivers on the signs and symptoms of hypoglycemia (see Warnings and Precautions (5.4)).

Acute Kidney Injury
Advise patients of the potential risk of dehydration due to gastrointestinal adverse reactions and to take precautions to avoid fluid depletion. Inform patients of the potential risk for worsening renal function, which in some cases may require dialysis (see Warnings and Precautions (5.5)).

Manufactured by:
Novo Nordisk A/S
DK-2880 Bagsvaerd, Denmark
Version: 16
VICTOZA® is a registered trademark of Novo Nordisk A/S.
For information about VICTOZA® contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainboro, NJ 08536
1-877-484-2869
© 2023 Novo Nordisk
US32170002 7/2023
Victoza® (liraglutide) injection 1.2 mg, 1.8 mg Medication Guide

What is the most important information I should know about Victoza®?

Victoza® may cause serious side effects, including:

- Possible thyroid tumors, including cancer. Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rats and mice, Victoza® and medicines that work like Victoza® caused thyroid tumors, including thyroid cancer. It is not known if Victoza® will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.

- Do not use Victoza® if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC), or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

What is Victoza®?

Victoza® is an injectable prescription medicine used:

- along with diet and exercise to lower blood sugar (glucose) in adults and children who are 10 years of age and older with type 2 diabetes mellitus.

- to reduce the risk of major cardiovascular events such as heart attack, stroke or death in adults with type 2 diabetes mellitus with known heart disease.

Victoza® is not for use in people with type 1 diabetes. It should not be used with other medicines that contain liraglutide. It is not known if Victoza® is safe and effective to lower blood sugar (glucose) in children under 10 years of age.

Who should not use Victoza®?

Do not use Victoza® if:

- you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

- you have had a serious allergic reaction to liraglutide or any of the ingredients in Victoza®. See the end of this Medication Guide for a complete list of ingredients in Victoza®.

Symptoms of a serious allergic reaction include:
- swelling of your face, lips, tongue or throat
- problems breathing or swallowing
- severe rash or itching
- fainting or feeling dizzy
- very rapid heartbeat

What should I tell my healthcare provider before using Victoza®?

Before using Victoza®, tell your healthcare provider if you have any other medical conditions, including if you:

- have or have had problems with your pancreas, kidneys, or liver.

- have severe problems with your stomach, such as slowed emptying of your stomach (gastraparesis) or problems with digesting food.

- are pregnant or plan to become pregnant. It is not known if Victoza® will harm your unborn baby. Tell your healthcare provider if you become pregnant while using Victoza®.

- are breastfeeding or plan to breastfeed. It is not known if Victoza® passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using Victoza®.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Victoza® may affect the way some medicines work and some medicines may affect the way Victoza® works.

Before using Victoza®, talk to your healthcare provider about low blood sugar and how to manage it. Tell your healthcare provider if you are taking other medicines to treat diabetes, including insulin or sulfonylureas.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use Victoza®?

- Read the Instructions for Use that comes with Victoza®.

- Use Victoza® exactly as your healthcare provider tells you to.

- Your healthcare provider should show you how to use Victoza® before you use it for the first time.

- Use Victoza® 1 time each day, at any time of the day.

- Victoza® may be taken with or without food.

- Victoza® is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. Do not inject Victoza® into a muscle (intramuscularly) or vein (intravenously).

- Change (rotate) your injection site within the area you choose with each injection to reduce your risk of getting lumps under the skin (cutaneous amyloidosis). Do not use the same site for each injection.

- Do not mix insulin and Victoza® together in the same injection.

- You may give an injection of Victoza® and insulin in the same body area (such as your stomach area), but not right next to each other.

- If you miss a dose of Victoza®, take the missed dose at the next scheduled dose. Do not take 2 doses of Victoza® at the same time.

- If you take too much Victoza®, call your healthcare provider right away. Taking too much Victoza® may cause severe nausea, severe vomiting, and low blood sugar (hypoglycemia).

- Do not share your Victoza® pen with other people, even if the needle has been changed.

- The Victoza® pen you are using should be thrown away 30 days after you start using it.

Your dose of Victoza® and other diabetes medicines may need to change because of:

- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

What are the possible side effects of Victoza®?

Victoza® may cause serious side effects, including:

- See “What is the most important information I should know about Victoza®?”

- Inflammation of your pancreas (pancreatitis). Stop using Victoza® and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.

- Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Victoza® with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin.

- High blood sugar. Victoza® does not control high blood sugar. If you have high blood sugar, you will need to take other medicines, such as insulin, to control your blood sugar.

- Kidney problems (kidney failure). In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse.

- Serious allergic reactions. Stop using Victoza® and get medical help right away, if you have any symptoms of a serious allergic reaction including:

- swelling of your face, lips, tongue or throat
- problems breathing or swallowing
- severe rash or itching
- fainting or feeling dizzy
- very rapid heartbeat

Kidney problems (kidney failure). In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse.

- Gallbladder problems. Gallbladder problems have happened in some people who take Victoza®. Tell your healthcare provider right away if you get symptoms of gallbladder problems which may include:

- pain in your upper stomach (abdomen)
- fever

- Clay-colored stools

The most common side effects of Victoza® may include: Nausea, diarrhea, vomiting, decreased appetite, indigestion and constipation. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of Victoza®.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Victoza® for a condition for which it was not prescribed. Do not give Victoza® to other people, even if they have the same symptoms that you have. It may harm them. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Victoza® that is written for health professionals.

What are the ingredients in Victoza®?

Active ingredient: liraglutide

Inactive ingredients: disodium phosphate dihydrate, propylene glycol, phenol and water for injection, hydrochloric acid or sodium hydroxide may be added to adjust pH

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 06/2022
**Routine Use**

**Step E. Check the Pen**
- Take your Victoza® pen from where it is stored.
- Wash hands with soap and water before use.
- Check pen label before each use to make sure it is your Victoza® pen.
- Pull off pen cap (See Figure H).
- Check Victoza® in the cartridge. The liquid should be clear, colorless and free of particles. If not, do not use.
- Wipe the rubber stopper with an alcohol swab.

**Step F. Attach the Needle**
- Remove protective tab from outer needle cap.
- Push outer needle cap containing the needle straight onto the pen, then screw needle on until secure (See Figure I).
- Pull off outer needle cap. Do not throw away (See Figure J).
- Pull off inner needle cap and throw away (See Figure K). A small droplet of liquid may appear. This is normal.

**Step G. Dial the Dose**
- Victoza® pen can give a dose of 0.6 mg (starting dose), 1.2 mg or 1.8 mg. Be sure that you know the dose of Victoza® that is prescribed for you.
- Turn the dose selector until your needed dose lines up with the pointer (0.6 mg, 1.2 mg or 1.8 mg) (See Figure L).
- You will hear a "click" every time you turn the dose selector. Do not set the dose by counting the number of clicks you hear.
- If you select a wrong dose, change it by turning the dose selector backwards or forwards until the correct dose lines up with the pointer. Be careful not to press the dose button when turning the dose selector. This may cause Victoza® to come out.

**Step H. Injecting the Dose**
- Insert needle into your skin in the stomach (abdomen), thigh or upper arm. Use the injection technique shown to you by your healthcare provider. Do not inject Victoza® into a vein or muscle.
- Press down on the center of the dose button to inject until 0 mg lines up with the pointer (See Figure M).
- Be careful not to touch the dose display with your other fingers. This may block the injection.
- Keep the dose button pressed down and make sure that you keep the needle under the skin for a full count of 6 seconds to make sure the full dose is injected. Keep your thumb on the injection button until you remove the needle from your skin (See Figure N).
- Change (rotate) your injection sites within the area you choose for each dose. Do not use the same injection site for each injection.

**Step I. Withdraw Needle**
- You may see a drop of Victoza® at the needle tip. This is normal and it does not affect the dose you just received. If blood appears after you take the needle out of your skin, apply light pressure, but do not rub the area (See Figure O).

**Step J. Remove and Dispose of the Needle**
- Carefully put the outer needle cap over the needle (See Figure P). Unscrew the needle.
- Safely remove the needle from your Victoza® pen after each use.
- Put your used VICTOZA® pen and needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and pens in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharp edges being able to come out
  - upright and stable during use
  - leak-resistant
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. Do not reuse or share your needles with other people. For more information about the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

**Caring for your Victoza® pen**
- After removing the needle, put the pen cap on your Victoza® pen and store your Victoza® pen without the needle attached (See Figure Q).
- Do not try to refill your Victoza® pen – it is prefilled and is disposable.
- Do not try to repair your pen or pull it apart.
- Keep your Victoza® pen away from dust, dirt and liquids.
- If cleaning is needed, wipe the outside of the pen with a clean, damp cloth.

**First read the Medication Guide that comes with your Victoza® single-patient-use pen and then read this Patient Instructions for Use for information about how to use your Victoza® pen the right way. These instructions do not take the place of talking with your healthcare provider about your medical condition or your treatment. Do not share your Victoza® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.**

Your Victoza® pen is a disposable single-patient-use prefilled pen injector that contains 3 mL of Victoza® and will deliver doses of 0.6 mg, 1.2 mg or 1.8 mg. The number of doses that you can take with a Victoza® pen depends on the dose of medicine that is prescribed for you. Your healthcare provider will tell you how much Victoza® to take. Victoza® pen should be used with Novo Nordisk disposable needles. Talk to your healthcare provider or pharmacist for more information about needles for your Victoza® pen.

**Important Information**
- Always use a new needle for each injection to prevent contamination.
- Always remove the needle after each injection, and store your pen without the needle attached. This reduces the risk of contamination, infection, leakage of liraglutide, blocked needles and inaccurate dosing.
- Keep your Victoza® pen and all medicines out of the reach of children.
- If you drop your Victoza® pen, repeat "First Time Use For Each New Pen" (steps A through D).
- Be careful not to bend or damage the needle.
- Do not use the cartridge scale to measure how much Victoza® to inject.
- Be careful when handling used needles to avoid needle stick injuries.
- You can use your Victoza® pen for up to 30 days after you use it the first time.

**First Time Use for Each New Pen**

**Step A. Check the Pen**
- Take your new Victoza® pen out of the refrigerator.
- Wash hands with soap and water before use.
- Check pen label before each use to make sure it is your Victoza® pen.
- Pull off pen cap (See Figure A).
- Check Victoza® in the cartridge. The liquid should be clear, colorless and free of particles. If not, do not use.
- Wipe the rubber stopper with an alcohol swab.

**Step B. Attach the Needle**
- Remove protective tab from outer needle cap (See Figure B).
- Push outer needle cap containing the needle straight onto the pen, then screw needle on until secure.
- Pull off outer needle cap (See Figure C). Do not throw away.
- Pull off inner needle cap and throw away (See Figure D). A small droplet of liquid may appear. This is normal.

**Step C. Dial to the Flow Check Symbol**
This step is done only **Once** for each new pen and is **Only** required the first time you use a new pen.
- Turn dose selector until flow check symbol (~) lines up with pointer (See Figure E). The flow check symbol does not administer the dose as prescribed by your healthcare provider.
- To select the dose prescribed by your healthcare provider, continue to Step G under "Routine Use".

**Step D. Prepare the Pen**
- Hold pen with needle pointing up.
- Tap cartridge gently with your finger a few times to bring any air bubbles to the top of the cartridge (See Figure F).
- Keep needle pointing up and press dose button until 9 mg lines up with pointer (See Figure G). Repeat steps C and D, up to 6 times, until a drop of Victoza® appears at the needle tip.
- If you still see no drop of Victoza®, use a new pen and contact Novo Nordisk at 1-877-484-2869.
- Continue to Step G under "Routine Use" ->

**Instructions For Use**

**Victoza® (liraglutide) injection**

**Victoza® Pen**
- Pen cap
- Rubber stopper
- Cartridge tip
- Cartridge scale
- Dose display
- Dose button
- Flow check symbol

**Needle (example)**
- Outer needle cap
- Inner needle cap
- Needle
- Protective tab

**If you are having problems using your Victoza® pen, call toll free 1-877-484-2869 or visit victoza.com.**
How should I store Victoza®?

**Before use:**
- Store your new, unused Victoza® pen in the refrigerator at 36°F to 46°F (2°C to 8°C).
- If Victoza® is stored outside of refrigeration (by mistake) prior to first use, it should be used or thrown away within 30 days.
- Do not freeze Victoza® or use Victoza® if it has been frozen. Do not store Victoza® near the refrigerator cooling element.

**Pen in use:**
- Use a Victoza® pen for only 30 days. Throw away a used Victoza® pen 30 days after you start using it, even if some medicine is left in the pen.
- Store your Victoza® pen at 59°F to 86°F (15°C to 30°C), or in a refrigerator at 36°F to 46°F (2°C to 8°C).
- When carrying the pen away from home, store the pen at a temperature between 59°F to 86°F (15°C to 30°C).
- If Victoza® has been exposed to temperatures above 86°F (30°C), it should be thrown away.
- Protect your Victoza® pen from heat and sunlight.
- Keep the pen cap on when your Victoza® pen is not in use.
- Always remove the needle after each injection and store your pen without the needle attached. This reduces the risk of contamination, infection, leakage and inaccurate dosing.